

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2004/033058

International filing date (day/month/year)
30.09.2004

Priority date (day/month/year)
01.10.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/16, A61K9/28, A61K47/32, A61K47/38, A61K47/14, A61K31/4439

Applicant
WYETH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/033058

IP20 Rec'd PCT/PTO 31 MAR 2006

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/033058

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 23 (with regard to industrial applicability)

because:

- ☒ the said international application, or the said claims Nos. 23 (with regard to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/033058

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	19
	No: Claims	1-18, 20-30
Inventive step (IS)	Yes: Claims	
	No: Claims	1-30
Industrial applicability (IA)	Yes: Claims	1-22, 24-30
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)

International application No.

AP20 Rec'd PCT/TO 31 MAR 2006
PCT/US2004/033058

SECTION III

1. Claim 23 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

SECTION V

2. References:

D1: WO 96/01624 A
D2: US-A-6 159 499
D3: US-B1-6 365 184
D4: US-A-5 997 903

3. Novelty (Art. 33(2) PCT)

- 3.1 D1 discloses enteric-coating-layered units of core material containing e.g. pantoprazole compressed into a tablet.

'The multiple unit tableted dosage form may be dispersed in an aqueous liquid and can be given to patients with swallowing disorders and in pediatrics. Such a suspension of dispersed enteric coating layered units of appropriate size can be used for oral administration and also for feeding through a naso-gastric tube.' (p. 9, l. 23-27).

The active may be formulated into a core material by extrusion / spheronization. The size of the formulated core material is between 0.1 and 4 mm, preferably between 0.1 and 2 mm. Binders, disintegrating agents and surfactants can be used (see p. 12, l. 9 and p. 11, l. 19-26).

Before applying enteric coating layer(s) onto the core material in the form of individual pellets, said pellets may optionally be covered with one or more separating layers. The material for separating layers can e.g. be *hydroxypropyl methylcellulose* (hypromellose) (p. 13).

Pellets covered with enteric coating layer(s) may further be covered with one or more

over-coating layer(s) (e.g. HPMC, p. 15/16).

(see in particular *example 2* in combination with the general disclosure of **D1**).

The amount of the over-coating layer in the examples falls within the ranges of claim 3.

D1 would be *prejudicial to the novelty* of the present claims with exception of claim 19.

3.2 **D2** discloses multiparticulates having

a core which comprises a plurality of nuclei and an active principle, e.g. pantoprazole, mixed together;

an intermediate layer surrounding the core (e.g. HPMC), and

an enteric layer surrounding the intermediate layer (e.g. methacrylic acid polymer).

The core is prepared by e.g. granulation; polysorbate 80 or sodium lauryl sulfate are added (col. 6, l. 7-36).

The composition may be in form of micro-tablets enclosed inside a capsule (col. 7, l. 37). A capsule may contain e.g. 16 micro-tablets (col. 7, l. 48); therefrom, it would appear that the size of the micro-tablets correspond to the size of the particulates of the present application.

3.3 **D3** discloses enteric coating multiparticulates of e.g. *pantoprazole* which may be filled into a capsule, tableted to obtain a multiple unit dosage form or dispersed in an aqueous liquid to be fed through a naso-gastric tube.

The proton pump inhibitor may be formulated into a core material (pref. 0.1 - 2 mm) with excipients, e.g. binders, surfactants by extrusion / spheronization. Binders are e.g. cellulose or PVP; sodium lauryl sulfate is mentioned as suitable surfactant (col. 9).

A separating layer (e.g. HPMC) may be applied onto the cores before covering with an enteric coating (e.g. methacrylic acid copolymers). An over-coating layer may be as well applied.

The general disclosure and in particular in context with *examples 3, 12 and 17* would *anticipate* the subject-matter of the present claims with exception of claim 19.

4. Inventive Step (Art. 33(3) PCT)

In view of the teaching of the cited prior art documents, the particular formulation defined in claim 19 would *not* be considered *inventive*.

5. Industrial Applicability (Art. 33(4) PCT)

5.1 The requirements of industrial applicability would be fulfilled for the subject-matter of claims 1-22 and 24-30.

5.2 For the assessment of the present claim 23 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

SECTION VI

6. Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO2004098577	18/11/2004	07/05/04	08/05/03

WO2004098577 discloses pellets comprising pantoprazole and various coatings.